

### IN THE CLAIMS

Please amend the claims as follows:

1. (Currently amended) A peptide comprising ~~SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, SEQ ID NO:13, SEQ ID NO:15, SEQ ID NO:16, or SEQ ID NO:17,~~ wherein the peptide can inhibit matrix metalloproteinase-2.

2. (Withdrawn) A composition comprising a therapeutically effective amount of peptide of formula I and a pharmaceutically acceptable carrier:



wherein

Xaa<sub>1</sub>, Xaa<sub>4</sub>, and Xaa<sub>6</sub> are separately each apolar amino acids;

Xaa<sub>2</sub> is a basic amino acid;

Xaa<sub>3</sub> is a cysteine-like amino acid;

Xaa<sub>5</sub> is a polar or aliphatic amino acid;

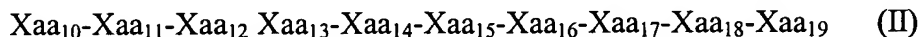
Xaa<sub>7</sub> is an acidic amino acid,

Xaa<sub>8</sub> is an aliphatic or polar amino acid;

Xaa<sub>9</sub> is an aliphatic, apolar or basic amino acid; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

3. (Withdrawn) A composition comprising a therapeutically effective amount of peptide of formula II and a pharmaceutically acceptable carrier:



wherein

Xaa<sub>10</sub> is a polar, acidic, basic or apolar amino acid;

Xaa<sub>11</sub> is a polar or aromatic amino acid;

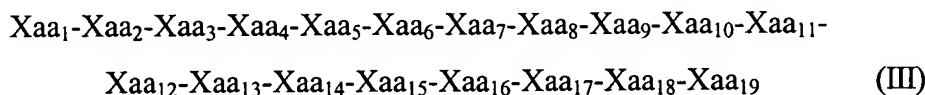
Xaa<sub>12</sub> is a polar, basic, aliphatic or apolar amino acid ;

Xaa<sub>13</sub> is an aromatic, aliphatic, polar or acidic amino acid;

Xaa<sub>14</sub> is an aromatic, apolar or polar amino acid;

Xaa<sub>15</sub> is an apolar or acidic amino acid;  
 Xaa<sub>16</sub> is a basic, a polar or an apolar amino acid;  
 Xaa<sub>17</sub> is a basic, a polar, an aliphatic, an apolar or an acidic amino acid;  
 Xaa<sub>18</sub> is an apolar or an aliphatic amino acid;  
 Xaa<sub>19</sub> is a basic or an aliphatic amino acid; and  
 wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

4. (Withdrawn) A composition comprising a therapeutically effective amount of peptide of formula III and a pharmaceutically acceptable carrier:

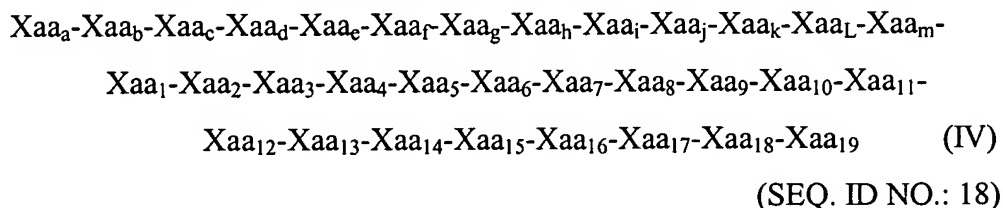


wherein

Xaa<sub>1</sub>, Xaa<sub>4</sub>, and Xaa<sub>6</sub> are separately each apolar amino acids;  
 Xaa<sub>2</sub> is a basic amino acid;  
 Xaa<sub>3</sub> is a cysteine-like amino acid;  
 Xaa<sub>5</sub> is a polar or aliphatic amino acid;  
 Xaa<sub>7</sub> is an acidic amino acid;  
 Xaa<sub>8</sub> is an aliphatic or polar amino acid;  
 Xaa<sub>9</sub> is an aliphatic, apolar or basic amino acid;  
 Xaa<sub>10</sub> is a polar, acidic, basic or apolar amino acid;  
 Xaa<sub>11</sub> is a polar or aromatic amino acid;  
 Xaa<sub>12</sub> is a polar, basic, aliphatic or apolar amino acid;  
 Xaa<sub>13</sub> is an aromatic, aliphatic, polar or acidic amino acid;  
 Xaa<sub>14</sub> is an aromatic, apolar or polar amino acid;  
 Xaa<sub>15</sub> is an apolar or acidic amino acid;  
 Xaa<sub>16</sub> is a basic, a polar or an apolar amino acid;  
 Xaa<sub>17</sub> is a basic, a polar, an aliphatic, an apolar or an acidic amino acid;  
 Xaa<sub>18</sub> is an apolar or an aliphatic amino acid;  
 Xaa<sub>19</sub> is a basic or an aliphatic amino acid; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

5. (Withdrawn) A composition that comprises a therapeutically effective amount of peptide of formula IV and a pharmaceutically acceptable carrier:



wherein:

Xaa <sub>a</sub> is proline;	Xaa <sub>1</sub> is proline;
Xaa <sub>b</sub> is glutamine or glutamic acid;	Xaa <sub>2</sub> is arginine;
Xaa <sub>c</sub> is threonine;	Xaa <sub>3</sub> is cysteine;
Xaa <sub>d</sub> is glycine;	Xaa <sub>4</sub> is glycine;
Xaa <sub>e</sub> is aspartic acid or glutamic acid;	Xaa <sub>5</sub> is valine or asparagine;
Xaa <sub>f</sub> is leucine;	Xaa <sub>6</sub> is proline;
Xaa <sub>g</sub> is aspartic acid;	Xaa <sub>7</sub> is aspartic acid;
Xaa <sub>h</sub> is glutamine or serine;	Xaa <sub>8</sub> is valine or leucine;
Xaa <sub>i</sub> is asparagine or alanine;	Xaa <sub>9</sub> is alanine or glycine;
Xaa <sub>j</sub> is threonine;	Xaa <sub>10</sub> is asparagine or arginine;
Xaa <sub>k</sub> is isoleucine or leucine;	Xaa <sub>11</sub> is tyrosine or
	phenylalanine;
Xaa <sub>L</sub> is glutamic acid or lysine;	Xaa <sub>12</sub> is asparagine or
	glutamine;
Xaa <sub>m</sub> is threonine or alanine;	Xaa <sub>13</sub> is phenylalanine or
	threonine;
Xaa <sub>n</sub> is methionine;	Xaa <sub>14</sub> is phenylalanine;
Xaa <sub>o</sub> is arginine;	Xaa <sub>15</sub> is proline or glutamic
	acid;
Xaa <sub>p</sub> is lysine or threonine;	Xaa <sub>16</sub> is arginine or glycine;
Xaa <sub>17</sub> is lysine or aspartic acid;	Xaa <sub>18</sub> is proline or leucine;
Xaa <sub>19</sub> is lysine; and	

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

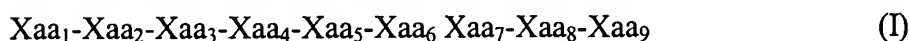
6. (Withdrawn) The composition of any one of claims 2-5, wherein an apolar amino acid is methionine, glycine or proline.
7. (Withdrawn) The composition of any one of claims 2-5, wherein a basic amino acid is histidine, lysine, arginine, 2,3-diaminopropionic acid, ornithine, homoarginine,  $\rho$ -aminophenylalanine, and 2,4-diaminobutyric acid.
8. (Withdrawn) The composition of any one of claims 2-5, wherein a cysteine-like amino acid is cysteine, homocysteine, penicillamine, or  $\beta$ -methyl cysteine.
9. (Withdrawn) The composition of any one of claims 2-5, wherein an aliphatic amino acid is alanine, valine, leucine, isoleucine, t-butylalanine, N-methylisoleucine, norleucine, N-methylvaline, cyclohexylalanine,  $\beta$ -alanine, N-methylglycine, or  $\alpha$ -aminoisobutyric acid.
10. (Withdrawn) The composition of any one of claims 2-5, wherein an acidic amino acid is aspartic acid or glutamic acid.
11. (Withdrawn) The composition of any one of claims 2-5, wherein a polar amino acid is asparagine, glutamine, serine, threonine, tyrosine, citrulline, N-acetyl lysine, methionine sulfoxide, or homoserine, or an apolar amino acid such as methionine, glycine or proline.
12. (Withdrawn) The composition of any one of claims 2-5, wherein an aromatic amino acid is phenylalanine, tyrosine, tryptophan, phenylglycine, naphthylalanine,  $\beta$ -2-thienylalanine, 1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid, 4-chlorophenylalanine, 2-fluorophenylalanine, 3-fluorophenylalanine, 4-fluorophenylalanine, pyridylalanine, or 3-benzothienyl alanine.
13. (Withdrawn) The composition of any one of claims 2-5 wherein the matrix metalloproteinase is any one of matrix metalloproteinase-1, matrix metalloproteinase-2, matrix

metalloproteinase-3, matrix metalloproteinase-4, matrix metalloproteinase-4, matrix metalloproteinase-5, matrix metalloproteinase-6, matrix metalloproteinase-7, matrix metalloproteinase-8, and matrix metalloproteinase-9, matrix metalloproteinase-10, matrix metalloproteinase-11, matrix metalloproteinase-12, or matrix metalloproteinase-13.

14. (Currently amended) A composition that comprises a therapeutically effective amount of peptide that comprises ~~SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7,~~ SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, ~~SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:13,~~ and a pharmaceutically acceptable carrier.

15. (Currently amended) The composition of claim 14 wherein the peptide can inhibit proteinase activity of any one of matrix metalloproteinase-1, matrix metalloproteinase-2, matrix metalloproteinase-3, matrix metalloproteinase-4, ~~matrix metalloproteinase-4,~~ matrix metalloproteinase-5, matrix metalloproteinase-6, matrix metalloproteinase-7, matrix metalloproteinase-8, and matrix metalloproteinase-9, matrix metalloproteinase-10, matrix metalloproteinase-11, matrix metalloproteinase-12, or matrix metalloproteinase 13.

16. (Withdrawn) A wound dressing that comprises a peptide of the formula I:



wherein

Xaa<sub>1</sub>, Xaa<sub>4</sub>, and Xaa<sub>6</sub> are separately each apolar amino acids;

Xaa<sub>2</sub> is a basic amino acid;

Xaa<sub>3</sub> is a cysteine-like amino acid;

Xaa<sub>5</sub> is a polar or aliphatic amino acid;

Xaa<sub>7</sub> is an acidic amino acid,

Xaa<sub>8</sub> is an aliphatic or polar amino acid;

Xaa<sub>9</sub> is an aliphatic, apolar or basic amino acid; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

## 17. (Withdrawn) A wound dressing that comprises a peptide of the formula II:



wherein

Xaa<sub>10</sub> is a polar, acidic, basic or apolar amino acid;

Xaa<sub>11</sub> is a polar or aromatic amino acid;

Xaa<sub>12</sub> is a polar, basic, aliphatic or apolar amino acid ;

Xaa<sub>13</sub> is an aromatic, aliphatic, polar or acidic amino acid;

Xaa<sub>14</sub> is an aromatic, apolar or polar amino acid;

Xaa<sub>15</sub> is an apolar or acidic amino acid;

Xaa<sub>16</sub> is a basic, a polar or an apolar amino acid;

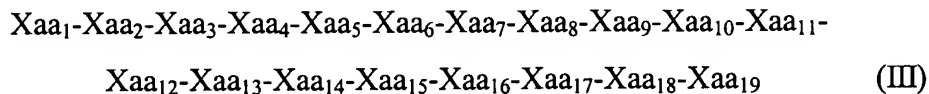
Xaa<sub>17</sub> is a basic, a polar, an aliphatic, an apolar or an acidic amino acid;

Xaa<sub>18</sub> is an apolar or an aliphatic amino acid;

Xaa<sub>19</sub> is a basic or an aliphatic amino acid; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

## 18. (Withdrawn) A wound dressing that comprises a peptide of formula III:



wherein

Xaa<sub>1</sub>, Xaa<sub>4</sub>, and Xaa<sub>6</sub> are separately each apolar amino acids;

Xaa<sub>2</sub> is a basic amino acid;

Xaa<sub>3</sub> is a cysteine-like amino acid;

Xaa<sub>5</sub> is a polar or aliphatic amino acid;

Xaa<sub>7</sub> is an acidic amino acid;

Xaa<sub>8</sub> is an aliphatic or polar amino acid;

Xaa<sub>9</sub> is an aliphatic, apolar or basic amino acid;

Xaa<sub>10</sub> is a polar, acidic, basic or apolar amino acid;

Xaa<sub>11</sub> is a polar or aromatic amino acid;

Xaa<sub>12</sub> is a polar, basic, aliphatic or apolar amino acid;

Xaa<sub>13</sub> is an aromatic, aliphatic, polar or acidic amino acid;

Xaa<sub>14</sub> is an aromatic, apolar or polar amino acid;

Xaa<sub>15</sub> is an apolar or acidic amino acid;

Xaa<sub>16</sub> is a basic, a polar or an apolar amino acid;

Xaa<sub>17</sub> is a basic, a polar, an aliphatic, an apolar or an acidic amino acid;

Xaa<sub>18</sub> is an apolar or an aliphatic amino acid;

Xaa<sub>19</sub> is a basic or an aliphatic amino acid; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

19. (Withdrawn) A wound dressing that comprises a peptide of formula IV:

Xaa<sub>a</sub>-Xaa<sub>b</sub>-Xaa<sub>c</sub>-Xaa<sub>d</sub>-Xaa<sub>e</sub>-Xaa<sub>f</sub>-Xaa<sub>g</sub>-Xaa<sub>h</sub>-Xaa<sub>i</sub>-Xaa<sub>j</sub>-Xaa<sub>k</sub>-Xaa<sub>L</sub>-Xaa<sub>m</sub>-

Xaa<sub>1</sub>-Xaa<sub>2</sub>-Xaa<sub>3</sub>-Xaa<sub>4</sub>-Xaa<sub>5</sub>-Xaa<sub>6</sub>-Xaa<sub>7</sub>-Xaa<sub>8</sub>-Xaa<sub>9</sub>-Xaa<sub>10</sub>-Xaa<sub>11</sub>-

Xaa<sub>12</sub>-Xaa<sub>13</sub>-Xaa<sub>14</sub>-Xaa<sub>15</sub>-Xaa<sub>16</sub>-Xaa<sub>17</sub>-Xaa<sub>18</sub>-Xaa<sub>19</sub> (IV)

(SEQ ID NO.: 18)

wherein:

Xaa<sub>a</sub> is proline;

Xaa<sub>1</sub> is proline;

Xaa<sub>b</sub> is glutamine or glutamic acid;

Xaa<sub>2</sub> is arginine;

Xaa<sub>c</sub> is threonine;

Xaa<sub>3</sub> is cysteine;

Xaa<sub>d</sub> is glycine;

Xaa<sub>4</sub> is glycine;

Xaa<sub>e</sub> is aspartic acid or glutamic acid;

Xaa<sub>5</sub> is valine or asparagine;

Xaa<sub>f</sub> is leucine;

Xaa<sub>6</sub> is proline;

Xaa<sub>g</sub> is aspartic acid;

Xaa<sub>7</sub> is aspartic acid;

Xaa<sub>h</sub> is glutamine or serine;

Xaa<sub>8</sub> is valine or leucine;

Xaa<sub>i</sub> is asparagine or alanine;

Xaa<sub>9</sub> is alanine or glycine;

Xaa<sub>j</sub> is threonine;

Xaa<sub>10</sub> is asparagine or arginine;

Xaa<sub>k</sub> is isoleucine or leucine;

Xaa<sub>11</sub> is tyrosine or

phenylalanine;

Xaa<sub>L</sub> is glutamic acid or lysine;

Xaa<sub>12</sub> is asparagine or

glutamine;

Xaa<sub>m</sub> is threonine or alanine;

Xaa<sub>13</sub> is phenylalanine or

threonine;

Xaa<sub>n</sub> is methionine;

Xaa<sub>14</sub> is phenylalanine;

Xaa<sub>o</sub> is arginine;

Xaa<sub>15</sub> is proline or glutamic

acid;

Xaa<sub>p</sub> is lysine or threonine;

Xaa<sub>16</sub> is arginine or glycine;

Xaa<sub>17</sub> is lysine or aspartic acid;

Xaa<sub>18</sub> is proline or leucine;

Xaa<sub>19</sub> is lysine; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.

20. (Withdrawn) The wound dressing of any one of claims 16-19 or 28, wherein an apolar amino acid is methionine, glycine or proline.

21. (Withdrawn) The wound dressing of any one of claims 16-19 or 28, wherein a basic amino acid is histidine, lysine, arginine, 2,3-diaminopropionic acid, ornithine, homoarginine,  $\rho$ -aminophenylalanine, and 2,4-diaminobutyric acid.

22. (Withdrawn) The wound dressing of any one of claims 16-19 or 28, wherein a cysteine-like amino acid is cysteine, homocysteine, penicillamine, or  $\beta$ -methyl cysteine.

23. (Withdrawn) The wound dressing of any one of claims 16-19 or 28, wherein an aliphatic amino acid is alanine, valine, leucine, isoleucine, t-butylalanine, N-methylisoleucine, norleucine, N-methylvaline, cyclohexylalanine,  $\beta$ -alanine, N-methylglycine, or  $\alpha$ -aminoisobutyric acid.

24. (Withdrawn) The wound dressing of any one of claims 16-19 or 28, wherein an acidic amino acid is aspartic acid or glutamic acid.

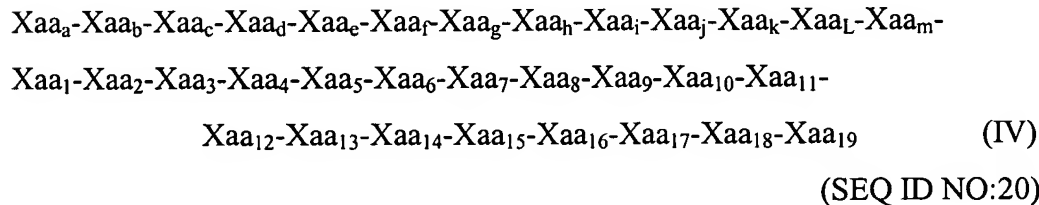
25. (Withdrawn) The wound dressing of any one of claims 16-19 or 28, wherein a polar amino acid is asparagine, glutamine, serine, threonine, tyrosine, citrulline, N-acetyl lysine, methionine sulfoxide, or homoserine, or an apolar amino acid such as methionine, glycine or proline.



26. (Withdrawn) The wound dressing of any one of claims 16-19 or 28, wherein an aromatic amino acid is phenylalanine, tyrosine, tryptophan, phenylglycine, naphthylalanine,  $\beta$ -2-thienylalanine, 1,2,3,4-tetrahydro-isoquinoline-3-carboxylic acid, 4-chlorophenylalanine, 2-fluorophenylalanine, 3-fluorophenylalanine, 4-fluorophenylalanine, pyridylalanine, or 3-benzothieryl alanine.

27. (Currently amended) A wound dressing that comprises a peptide comprising ~~SEQ ID NO:1, SEQ ID NO:2, SEQ ID NO:3, SEQ ID NO:4, SEQ ID NO:5, SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, or SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:12, or SEQ ID NO:13,~~ wherein the peptide can inhibit a matrix metalloproteinase.

28. (Withdrawn) A composition that comprises a therapeutically effective amount of peptide of formula IV and a pharmaceutically acceptable carrier:



wherein:

Xaa<sub>1</sub>, Xaa<sub>4</sub>, and Xaa<sub>6</sub> are separately each apolar amino acids;

Xaa<sub>2</sub> is a basic amino acid;

Xaa<sub>3</sub> is a cysteine-like amino acid;

Xaa<sub>5</sub> is a polar or aliphatic amino acid;

Xaa<sub>7</sub> is an acidic amino acid,

Xaa<sub>8</sub> is an aliphatic or polar amino acid;

Xaa<sub>9</sub> is an aliphatic, apolar or basic amino acid; and

Xaa<sub>10</sub> is a polar, acidic, basic or apolar amino acid;

Xaa<sub>11</sub> is a polar or aromatic amino acid;

Xaa<sub>12</sub> is a polar, basic, aliphatic or apolar amino acid ;

Xaa<sub>13</sub> is an aromatic, aliphatic, polar or acidic amino acid;

**RESPONSE TO RESTRICTION REQUIRMENT**

Serial Number: 10/032,376

Filing Date: December 21, 2001

Title: METALLOPROTEINASE INHIBITORS FOR WOUND HEALING

---

Page 11

Dkt: 1443.008US1

Xaa<sub>14</sub> is an aromatic, apolar or polar amino acid;

Xaa<sub>15</sub> is an apolar or acidic amino acid;

Xaa<sub>16</sub> is a basic, a polar or an apolar amino acid;

Xaa<sub>17</sub> is a basic, a polar, an aliphatic, an apolar or an acidic amino acid;

Xaa<sub>18</sub> is an apolar or an aliphatic amino acid;

Xaa<sub>19</sub> is a basic or an aliphatic amino acid;

Xaa<sub>a</sub> is proline;

Xaa<sub>b</sub> is glutamine or glutamic acid;

Xaa<sub>c</sub> is threonine;

Xaa<sub>d</sub> is glycine;

Xaa<sub>e</sub> is aspartic acid or glutamic acid;

Xaa<sub>f</sub> is leucine;

Xaa<sub>g</sub> is aspartic acid;

Xaa<sub>h</sub> is glutamine or serine;

Xaa<sub>i</sub> is asparagine or alanine;

Xaa<sub>j</sub> is threonine;

Xaa<sub>k</sub> is isoleucine or leucine;

Xaa<sub>L</sub> is glutamic acid or lysine;

Xaa<sub>m</sub> is threonine or alanine;

Xaa<sub>n</sub> is methionine;

Xaa<sub>o</sub> is arginine;

Xaa<sub>p</sub> is lysine or threonine; and

wherein the peptide is capable of inhibiting the activity of a matrix metalloproteinase.